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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/063,718	05/08/2002	Audrey Goddard	P3230R1C001-168	8618

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KNOBBE, MARTENS, OLSON & BEAR, LLP
2040 MAIN STREET
IRVINE, CA 92614

EXAMINER	
WEGERT, SANDRA L	

ART UNIT	PAPER NUMBER
1647	

DATE MAILED: 07/08/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/063,718	GODDARD ET AL.	
	Examiner	Art Unit	
	Sandra Wegert	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 April 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *4-6,11-14 and 16-31* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *4-6,11-14 and 16-31* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *08 May 2002* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *4/28/05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Detailed Action

Status of Application, Amendments, and/or Claims

A request for continued examination (RCE) under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. This application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid.

The Response, Information Disclosure Statement, and Amendments, all submitted 28 April 2005, have been entered. Claims 4, 5, 12 and 13 are amended. Claims 1-3, 7-10 and 15 are canceled. Claims 21-31 are new.

Claims 4-6, 11-14 and 16-31 are under examination in the Instant Application.

The text of those sections of Title 35, U.S. Code, not included in this action can be found in a prior Office action.

Withdrawn Objections And/or Rejections

Continuity

The objection to the Specification for not complying with one or more conditions for receiving the benefit of an earlier filing date under 35 U.S.C. 119, is *withdrawn,* based on Applicant's arguments (page 7, 28 April 2005). The filing date of the PCT Application (24 August 2000) is considered as the priority date.

Maintained/New Objections and/or Rejections

35 U.S.C. § 101/112, first paragraph-, Lack of Utility, Enablement.

Claims 4-6, 11-14 and 16-31 are rejected under 35 U.S.C. 101, as lacking utility. The reasons for this rejection under *35 U.S.C. § 101* are set forth at pages 4-10 of the previous Office Action (27 January 2005). Claims 4-6, 11-14 and 16-31 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility for the reasons set forth in the previous Office Action (27 January 2005), one skilled in the art clearly would not know how to use the claimed invention.

Applicants argue (*Remarks*, 28 April 2005, page 6 and throughout) that the results presented in the instant Specification are enabling for nucleic acids encoding the polypeptide of SEQ ID NO: 94. They argue that the PRO1328 nucleic acid is a diagnostic marker for *melanoma* and *normal lung* tissue, and point to the results of the assay which showed transcription of the PRO1328 DNA in one normal tissue versus cancerous and one cancerous tissue versus normal. Applicants point out that the PRO1328 data of Example 18 refers to *transcription data*, not DNA amplification data (Response, page 12 and throughout).

Applicant's arguments (28 April 2005) have been fully considered but are not found to be persuasive for the following reasons:

In the instant case, the specification provides data showing an indeterminate increase in mRNA in one normal tissue and one tumor tissue (see Example 18, Specification). However,

there is no evidence regarding whether or not PRO1328 polypeptide levels are also increased in lung tissue versus lung tumor or in melanoma tissue. The literature cautions researchers against drawing conclusions based on small changes in transcript expression levels between normal and cancerous tissue. For example, Hu et al. (2003, Journal of Proteome Research 2: 405-412) analyzed 2286 genes that showed a greater than 1-fold difference in mean expression level between breast cancer samples and normal samples in a microarray (p. 408, middle of right column). Hu et al. discovered that, for genes displaying a 5-fold change or less in tumors compared to normal, there was no evidence of a correlation between altered gene expression and a known role in the disease. However, among genes with a 10-fold or more change in expression level, there was a strong and significant correlation between expression level and a published role in the disease (see discussion section).

Given the small increase in transcription of PRO1328 DNA, and the evidence provided by the current literature, it is clear that one skilled in the art would not assume that a small increase in message would enable use of the polynucleotide as a diagnostic tool. Further research needs to be done to determine whether the small increase in PRO1328 message supports a role for the peptide in detecting or treating cancerous tissue; an opposite role, or none at all, has been suggested by the instant disclosure. The requirement for further research makes it clear that the asserted utility is not yet in currently available form, i.e., it is not substantial. This further experimentation is part of the act of invention and until it has been undertaken, Applicant's claimed invention is incomplete. As discussed in Brenner v. Manson, (1966, 383 U.S. 519, 148 USPQ 689), the court held that:

> "The basic quid pro quo contemplated by the Constitution and the Congress for granting a patent monopoly is the benefit derived by the public from an invention

> with substantial utility", "[u]nless and until a process is refined and developed to this point-where specific benefit exists in currently available form-there is insufficient justification for permitting an applicant to engross what may prove to be a broad field", and,
>
> "a patent is not a hunting license", "[i]t is not a reward for the search, but compensation for its successful conclusion."

Accordingly, the Specification's assertions that the claimed PRO1328 nucleic acid has utility in the fields of cancer diagnostics and cancer therapeutics are not substantial.

There is no evidentiary support that PRO1328 is involved in the etiology of cancer in the one tumor sample and one normal sample disclosed in the instant Application. Furthermore, as noted above, the increase in PRO1328 message in normal tissue points away from its role in a disease. At any rate, one negative result and one positive result is too little data to make a conclusion about PRO1328 and cancer. The *specific* function of the PRO1328 polynucleotide has not been disclosed by Applicants or by recent research. Finally, it is noted that the literature cautions researchers from drawing conclusions based on small changes in expression levels between normal and cancerous tissue (see Hu et al., 2003, Journal of Proteome Research 2:405-412, as discussed above).

Applicants discuss (Response, 28 April 2005, page 9 and throughout) points from case law in reference to the utility rejection, most of which the examiner agrees with. However, the fact patterns of the cases cited have little connection with utility/enablement as applied to the instant Application. Whatever the asserted specific utility might be - diagnosis of cancer, for example- it is **not** "more likely than not" (In re Oetiker, 1992, 977 F2d 1443, 1445, 24 USPQ2d) or true "to a reasonable probability" (Fujikawa v. Wattanasin, 1996, 93 F3d 1559, 39 USPQ2d 1895) since it is just as likely that PRO1328 can be used to "diagnose" normal tissue.

Applicants discuss the Declarations submitted previously under 35 USC §1.132 to explain how data were gathered, etc. For example, the Declaration from Dr. Grimaldi explains that data from several of the same tissues are pooled. This results in a presumed difference of expression between the positive and negative tissue of 2-fold.

Applicant's arguments (28 April 2005) have been fully considered but are not found to be persuasive for the following reasons:

As discussed in the previous Office Action (27 January 2005), a 2-fold increase is not large and may be less likely to indicate disease (Hu, et al, 2003, Journal of Proteome Research 2:405-412), or may be sufficient (Applicant's Response, page 14). However, the type or magnitude of increase is not at issue in this case. All that is known about PRO1328 is that it is increased in one normal pooled tissue and one tumor tissue. It cannot be determined what the function of PRO1328 is in the tissue; certainly the tissue provides no clues. It is hard to conceive of a specific and substantial utility for a nucleic acid encoding a protein for which so little data or information is given. For example, why were other tissues not tested, as was the case for other PRO polynucleotides? What might be the connection between one normal tissue and one cancerous tissue that would provide clues to the function of PRO1328?

Applicants do not know the function of the PRO1328 polynucleotide or polypeptide. For this reason, detecting the PRO1328 mRNA has no specific function, since it is not useful to a polynucleotide or protein for which a function has not yet been identified, and additionally might be underexpressed in one cancer and overexpressed in another. Since the asserted utility for PRO1328 is not in currently available form, the asserted utility is not substantial.

Conclusion

No claims are allowed.

Advisory information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sandra Wegert whose telephone number is (571) 272-0895. The examiner can normally be reached Monday - Friday from 9:00 AM to 5:00 PM (Eastern Time). If attempts to reach the examiner by telephone are unsuccessful, the Examiner's supervisor, Brenda Brumback, can be reached at (571) 272-0961.

The fax number for the organization where this application or proceeding is assigned is 571-273-8300. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

SLW
30 June 2005

JANET ANDRES
PRIMARY EXAMINER